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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4 -33624A/GLT	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/EP2004/003737	International filing date *(day/month/year)* 07.04.2004	Priority date *(day/month/year)* 08.04.2003
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant GENOVA, LTD. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.11.2004	22.04.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Telephone No. +49 89 2399- 7490 WEILAND

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/003737

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-124 as originally filed

   Claims, Numbers

   1-16 as originally filed

   Drawings, Sheets

   1/5-5/5 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 14-16 (with respect to industrial applicability), 1-16 (partially)

because:

☒ the said international application, or the said claims Nos. 14-16 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-16 (partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-16 (partially) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7, 11, 12, 14-16
	No:	Claims	8, 9, 10, 13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

The following documents (D) are referred to in this opinion; the numbering will be adhered to the rest of the procedure:

D1: WO-A-9830588
D2: WO-A-9817808

SECTION III

1. The International Searching Authority has raised the objection of lack of unity and claims 1-16 have been searched only as far they relate to colipase (SEQ ID Nos 1-5). Therefore, the examination can only be carried out for claims 1-16 as far they relate to SEQ ID nos 1-5 (Rule 66(1)(e) PCT).

2. Claims 14-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION IV

3. This International searching Authority found multiple (groups of) inventions in this Internatinal application, as follows:

   Claims: 1-16 (partially)

   Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of a treatment etc. using SEQ ID Nos 1-5 involving colipase (Invention I), SEQ ID Nos 6-10 involving eosinophil-derived neurotoxin (invention II), SEQ ID Nos 11-14 involving human epididymal secretory protein (invention III), SEQ ID Nos 15-23 involving Defensin I (invention IV), SEQ ID Nos 24-28 involving plasminogen-related protein B (invention V).

   The authority in charge of the International Preliminary Examination considers that the present set of claims lacks unity (Rule 13.1 PCT) for the following reasons.

   The problem to be solved in the present application is the provision of markers for

cardiovascular disorders. The use of the proteins mentioned in claim 1 provides 5 solutions to the above problem. However, WO0206840, WO03023397, US6503540 (herein referred to as D1, D2 and D3, relevant passages as cited in the search report) disclose proteins that can be used as markers in cardiovascular disorders. Said markers disclose a non-exhaustive list of such markers.

In the light of D1 to D3, each document taken alone, the above identified single general concept is not novel and inventive and can thus not be the single general inventive concept as required by Rule 13.1 PCT. The present application is therefore considered not to fulfill the requirements of unity as laid down in Rule 13.1 PCT.

No other technical features could be identified that form a technical relationship among each of the separate inventions claimed and which could be considered as special technical features within the meaning of Rule 13.2 PCT.

The invention first mentioned in the claims (involving SEQ ID NOs 1-5, relating to colipase and fragments thereof, has been searched.

The searches for subjects 2-5 represent a major extra search burden. In consequence the applicant is invited to pay 4 addition search fees, for each of the following proteins used in ncardiovascular disorders.

2) eosinophil-derived neurotoxin (SEQ ID NOs 6-10)
3) Human Epididymal secretory protein (SEQ ID NOs 11-14)
4) defnsin I (SEQ ID NOs 15-23)
5) plasminogen-related protein B (SEQ ID NOs 24-28)

With regard to the decision T110/82 concerning the relationship between the interests of a national procedure up to grant, in which interconnected matter should not needlessly be split up nor unrelated inventions lumped together for the purpose of saving fees, in particular since the expense for the procedure for such cases must be partly borne by the fees levied for other applications, the present application has been split up as above, based on the different charactering features of these claimed inventions pursuant to Article 17(3)(a) PCT.

SECTION V

4. Novelty (Article 33(2) PCT)

4.1 The subject matter of claims 8, 9, 10 and 13 is anticipated by D1 and D2 and is therefore not novel.

D1 (abstract; page 3, paragraph 6) describes specific pancreatic lipase inhibitors in the treatment and prevention of cardiovascular diseases ("polypeptide", modulator" according to claims 8 and 13).

D2 (abstract; page 24, paragraph 10; page 11, paragraph 1-4) describes the production of recombinant co-lipases and pancreatic lipases and antibodies directed therefrom ("antibody" according to claims 9 and 10) and its use in diagnostic methods by measuring an increase in a sample due to a certain pathology.

4.2 The subject matter of claims 1-7, 11, 12 and 14-16 is not disclosed in the prior art documents and is therefore novel.

5. Inventive Step

5.1 The subject matter of claims 1-7, 11, 12 and 14-16 is not inventive (Articel 33(3) PCT).

D2 is considered to be the closest prior art document. Claims 1, 2, 13, 14 and 16 differ from D2 in that said methods relate SEQ ID Nos 1 and 2 to cardiovascular diseases.

The technical problem to be solved would reside in the application of colipase in alternative diseases.

The skilled person, equipped with the knowledge of D2, would be motivated to arrive at the subject matter of said claims, since D1 describes the involvement of colipases in cardiovascular diseases.

Therefore, claims 1-7, 11, 12 and 14-16 do not involve an inventive step.

5.2 Dependent claims 11 and 12 do not contain any features which, in combination with the features of claim 10 to which they refer, meet the requirements of the PCT in respect of inventive step, since they can be considered as mere alternatives without resulting in any unexpected effect whatsoever.

6. For the assessment of the present claims 14-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT contracting states. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in a medical treatment and the use of such compound for the manufacture of a medicament for new medical treatment.

In the above mentioned context the passages "administering a candidate agent..." or "obtaining a pre-administration..." in claims 14 and 16 is considered to cover treatment by therapy.